REMARKS

Claims 1-40 are pending. Claims 1-10 and 14-24 are under examination. Claims 1, 2 and 15 have been amended. New claims 41-43 have been added. Support for the amendments and new claims can be found throughout the specification and the claims as filed. In particular, support for new claims 41-43 can be found, for example, in original claims 1, 14 and 28, on page 16, line 14, to page 20, line 23, and in Examples VI-XI. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Applicant appreciates the Examiner's reconsideration of the restriction requirement and rejoining of the claims of Group IV with the claims of Group I.

Regarding Objections to the Specification

Regarding the priority claim, the first paragraph has been amended to reflect the parent provisional application serial number. Regarding the objection to the abstract, the abstract has been amended to delete the term "comprising" as suggested by the Examiner. Accordingly, these objections to the specification are respectfully requested to be withdrawn.

Rejection Under 35 U.S.C. § 101

The rejection of claims 1-10 under 35 U.S.C. § 112, second paragraph, as allegedly directed to non-statutory subject matter is respectfully traversed. Applicant respectfully submits that claims 1-10 are directed to statutory subject matter. Nevertheless, claim 1 has been amended to recite a cell transfected with the variant nucleic acids, as requested by the Examiner. Accordingly, it is respectfully requested that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 1-10 and 14-24 under 354 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Applicant respectfully submits that claims 1-10 and 14-24 are clear and definite.

With regard to claims 1, the Office Action indicates that the claims are indefinite for recitation that the variant nucleic acids are "being expressed." Claim 1 has been amended to recite that each cell expresses a single variant nucleic acid of the population of variant nucleic acids. It is respectfully submitted that such a recitation refers to a characterization of the claimed cell composition. Accordingly, it is respectfully submitted that claim 1 and dependent claims 3, 4, 16 and 22-24 are

clear and definite, and it is respectfully requested that this rejection be withdrawn.

With regard to claims 2 and 15, these claims have been amended to recite that the variant nucleic acids encode polypeptides having predetermined amino acid changes at preselected positions relative to a parent amino acid sequence. Thus, antecedent basis is provided for the recitation of "amino acid." The amino acid changes are relative to a parent amino acid sequence. With regard to the term "predetermined," the specification teaches that variants can be generated by introducing amino acid changes at predetermined positions using a variety of methods including, for example, site-directed mutagenesis and codon-based synthesis (see, for example, page 34, line 4, to page 38, line 17). Based on the teachings in the specification and what one skilled in the art would have known regarding the term "predetermined," Applicant respectfully submits that these claims are clear and definite.

Rejections Under 35 U.S.C. § 102

The rejection of claims 1, 3-10, 14 and 16-24 under 35 U.S.C. § 102(b) as allegedly anticipated by Bouhassira et al., Blood 90:3332-3344 (1997), is respectfully traversed. Applicant respectfully submits

that claims 1, 3-10, 14 and 16-24 are novel over Bouhassira et al.

Applicant submits that Bouhassira et al. does not teach the claimed cell compositions containing a population of non-yeast eukaryotic cells transfected with a diverse population of about 10 or more variant nucleic acids, wherein each cell expresses a single variant nucleic acid of the population of variant nucleic acids and wherein the variant nucleic acid is located within each cell at an identical site in the genome. At best, the reference describes the insertion of five cassettes with various hypersensitive sites of the β-globin locus control region. Absent such a teaching of the claimed cell composition, Bouhassira et al. cannot anticipate the claims. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1-10 and 14-24 under 35 U.S.C. § 102(b) as allegedly anticipated by Biard-Piechaczyk et al., Human Antibodies 9:67-77 (1999), is respectfully traversed. Applicant respectfully submits that claims 1-10 and 14-24 are novel over Biard-Piechaczyk et al.

Applicant submits that Biard-Piechaczyk et al. does not teach the claimed cell compositions containing a

population of non-yeast eukaryotic cells transfected with a diverse population of about 10 or more variant nucleic acids, wherein each cell expresses a single variant nucleic acid of the population of variant nucleic acids and wherein the variant nucleic acid is located within each cell at an identical site in the genome. At best, this reference describes the use of an antibody Fv fragment library. Absent a teaching of the claimed cell composition, Biard-Piechaczyk et al. cannot anticipate the claims. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1-4, 10, 14-16 and 22-24 under 35 U.S.C. § 102(b) as allegedly anticipated by Le et al., Nucl. Acids Res. 27:4703-4709 (1999), or Thomas et al., Cell 44:419-428 (1986), is respectfully traversed. Applicant respectfully submits that claims 1-4, 10, 14-16 and 22-24 are novel over Le et al. or Thomas et al.

Applicant submits that neither Le et al. nor Thomas et al. teaches the claimed cell compositions containing a population of non-yeast eukaryotic cells transfected with a diverse population of about 10 or more variant nucleic acids, wherein each cell expresses a single variant nucleic acid of the population of variant nucleic acids and wherein the variant nucleic acid is located within each cell at an identical site in the genome. At best, Le et al. describes nuclear targeting domains of Cre

but not a population of variant nucleic acids. Thomas et al., at best, describes the use of a neo plasmid and two derivative plasmids with an amber mutation and deletion mutant of neo. However, neither Le et al. nor Thomas et al. teaches the claimed cell composition and therefore cannot anticipate the claims. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1-6, 8, 10, 14-17, 20 and 22-24 under 35 U.S.C. § 102(a) as allegedly anticipated by Choi et al., Nucl. Acids Res. 28:e19 (2000), is respectfully traversed. Applicant respectfully submits that claims 1-6, 8, 10, 14-17, 20 and 22-24 under are novel over Choi et al.

Applicant submits that Choi et al. does not teach the claimed cell compositions containing a population of non-yeast eukaryotic cells transfected with a diverse population of about 10 or more variant nucleic acids, wherein each cell expresses a single variant nucleic acid of the population of variant nucleic acids and wherein the variant nucleic acid is located within each cell at an identical site in the genome. At best, Choi et al. appears to describe a BAC vector and expression of a BAC library but does not teach the claimed cell composition. Absent such a teaching, Choi et al. cannot anticipate the claims. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1, 10, 14 and 24 under 35 U.S.C. § 102(e) as allegedly anticipated by Treco et al., U.S. patent No. 6,063,630, or Stemmer, U.S. patent No. 6,132,970, is respectfully traversed. Applicant respectfully submits that claims 1, 10, 14 and 24 are novel over Treco et al. or Stemmer.

Applicant submits that neither Treco et al. nor Stemmer teaches the claimed cell compositions containing a population of non-yeast eukaryotic cells transfected with a diverse population of about 10 or more variant nucleic acids, wherein each cell expresses a single variant nucleic acid of the population of variant nucleic acids and wherein the variant nucleic acid is located within each cell at an identical site in the genome. At best, Treco et al. appears to describe the use of homologous recombination to introduce a gene of interest into genomic DNA. Regarding Stemmer, this reference does not teach the claimed cell composition containing variant nucleic acids. Absent a teaching of the claimed cell composition, neither Treco et al. nor Stemmer anticipates the claims. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

CONCLUSION

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

Respectfully submitted,

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